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EXAMINER	
STEELE, AMBER D	
ART UNIT	PAPER NUMBER
1639	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/658,632	CHENCHIK, ALEX	
	Examiner	Art Unit	
	AMBER D. STEELE	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 February 2009 and 22 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18,21-24,26-28,30-34 and 36-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18,21-24,26-28,30-34 and 36-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 January 2004 and February 25, 2009* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/25/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 1-23 were originally filed on September 8, 2003.

The amendment to the claims received on October 24, 2007 amended claim 17, canceled claims 1-16, and added new claims 24-28.

The amendment to the claims received on February 20, 2008 canceled claim 17, amended claims 18-27, and added new claim 29.

The amendment to the claims received on June 6, 2008 canceled claim 29.

The amendment received on February 25, 2009 amended claims 18, 23, 24, 26, and 27, canceled claims 19-20 and 25, and added new claims 30-38.

The amendment received on June 22, 2009 canceled claim 35.

Claims 18, 21-24, 26-28, 30-34, and 36-38 are currently pending and under consideration.

Election/Restrictions

2. Applicant's election of Group I (previous claims 18-28) in the reply filed on June 6, 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. Applicant's election of 1000 effector sequences as the species of number and siRNA as the species of effector sequence in the reply filed on June 6, 2008 is acknowledged. Because

applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

4. It is noted that applicants failed to elect a single, specific species for species A-D (see restriction mailed on May 22, 2009; see response received on June 22, 2009). However, upon further consideration the species requirement is withdrawn.

Priority

5. The priority date for the present application is the filing date of the present application (September 8, 2003).

Information Disclosure Statement

6. The information disclosure statement (IDS) submitted on February 25, 2009 is being considered by the examiner. It is noted that applicants provided a date for Robinson et al. However, the full citation should be provided in an IDS. The Jensen reference will not be considered until publication information is provided on an IDS.

Withdrawn Objection

7. The objection to the drawings regarding the lack of SEQ ID NOs: in Figures 9, 10, and 12 is withdrawn in view of the amendments to the drawings received on February 25, 2009.

New Rejection Necessitated by Amendment

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 18, 21-24, 26-28, 30-34, and 36-38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a **new matter** rejection.

Applicants are respectfully reminded that applicant should specifically point out the support for any amendments made to the disclosure (see MPEP § 2163).

Support in the originally filed specification for new claims 30-34 and 36-38 was not provided. Support in the originally filed specification for "siRNAs which are 19 to 27 nucleotides in length" (see present claim 24) and "each nucleic acid sequence…has a length of at least 70 nucleotides" (see present claims 26 and 27) was not provided.

The examiner of record found the following disclosures in the originally filed specification: short siRNAs of 19-29 nucleotides in length (i.e. different range than 19 to 27; see paragraph 5).

The following were not found in the originally filed specification: siRNA of 19 to 27 nucleotides in length, nucleic acid sequence has a length of at least 70 nucleotides, sense sequence of 19 to 27 nucleotides in length, antisense sequence of 19 to 27 nucleotides in length, loop sequence of 4 to 18 nucleotides in length, at least 19 nucleotides complementary to mammalian mRNA, expression vectors of present claim 32 (LTR from HIV, FIV, MMLV, and MSCV was found in paragraph 43, but recitation of a complete viral expression vector from the Markush recited in present claim 32 was not found), etc. Please note: all new claim limitations were not searched in the originally filed specification.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 18, 21-24, 26-28, 30-34, and 36-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. One of skill in the art would not be able to determine the scope of the presently claimed invention. For example, independent claims 26, 27, 36, and 37 require nucleic acid effector sequences of at least 70 nucleotides in length. However, claims 24, 30, 34, 36, and 37 require sequences which are less than 70 nucleotides in length (i.e. if double stranded – maximum length is 27 nucleotides with a loop region of 18, even if single stranded majority of sequences would be less than 70 nucleotides e.g. 20 NA sense, 20 NA antisense, 18 NA loop, etc.).

Maintained Rejections

Claim Rejections - 35 USC § 112

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 18, 21-24, 26-28, 30-34, and 36-38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the

Examination of Patent Applications under the 35 USC 112, first paragraph "Written Description" requirement, Federal Register, Vol. 66, No. 4 pages 1099-1111, Friday January 5, 2001. This is a **written description** rejection.

Independent claims 26, 27, 36, and 37 are drawn to a method for making a packaged viral effector library comprising (a) synthesizing a set of at least 100 different effector nucleic acid sequences on a surface of a microarray wherein each nucleic acid sequence has a specific sequence and is synthesized in a specific location of the surface, (b) detaching the set of nucleic acid sequences from the microarray, (c) amplifying the detached set of nucleic acid sequences from the microarray via PCR, and (d) cloning the defined set of nucleic acid sequences into viral expression vectors to produce a library of effector constructs and variations thereof. The invention as claimed encompasses all known nucleic acid sequences and viral expression vectors and all potential nucleic acid sequences and viral expression vectors since virtually any nucleic acid sequence can be inserted into a viral expression vector. The elected species of siRNA (also see present claims 23 and 24) and the requirement for 100 or 1,000 heterogenous siRNA further exacerbates the lack of written description because the specification does not disclose a single siRNA. The claimed invention does not include any structural information regarding the nucleic acid except that the nucleic acid encodes for siRNA (see claims 23 and 24; functional limitation). In addition, the claimed invention does not include any structural information regarding the viral vector except that the vectors can be lentiviral (see claims 21-22).

The specification teaches lentiviruses including HIV, visan-maedi, CAE, EIAV, FIV, BIV, and SIV (please refer to paragraph 40). In addition, the specification also teaches utilizing the pL-reporter lentiviral backbone, pLSLP which is similar to other known retroviral vectors

(please refer to paragraphs 78-79; Figures 3, 9). Furthermore, the specification is silent regarding a single, specific species of nucleic acid which encodes siRNA much less at least 100 or 1,000 heterogenous nucleic acid sequences. In particular, the specification refers to a genus of siRNAs which are 19 or 27 bp in length (see paragraph 80 for example). Furthermore, the specification does not teach if any of the generic siRNA discussed actually function as siRNA. Therefore, one skilled in the relevant art would not reasonably conclude that the Applicants had possession of the invention as claimed since the structural limitations are not included in the claims.

See Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was *in possession of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See page 1116.).

With the exception of the specific vectors disclosed in the specification, the skilled artisan cannot envision the method of independent claims 26, 27, 36, or 37, particularly wherein the product produced via the method as claimed requires at least 100 or 1,000 heterogenous siRNAs. For example Li et al., 2007, Predicting siRNA efficiency, Cell. Mol. Life Sci., 64: 1785-1792 teach that the efficiency of siRNA is dependent on the siRNA sequence, siRNA secondary structure, mRNA (i.e. target) secondary structure, etc. and that off-target effects can prevent the use of siRNA as treatments, etc. (see page 1787-1788). Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen

Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class wherein the specification provided only the bovine sequence.

Arguments and Response

14. Applicants' arguments directed to the rejection under 35 USC 112, first/second paragraph (written description), for claims 18, 21-24, 26-28, 30-34, and 36-38 were considered but are not persuasive for the following reasons.

Applicants contend that the application as originally filed provides adequate written description for the presently claimed inventions. Applicants specifically refer to Figure 1 which shows (a) effector library construction, (b) target cells transduced with the effector library, (c) desired cell phenotype is selected, and (d) the sequence of the siRNA is identified.

Applicants' arguments are not convincing since the originally filed specification fails to disclose a single siRNA. Regarding Figure 1, this is a schematic diagram of the method only and does not provide adequate written description for the presently claimed methods regarding the reagents utilized and the final products.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. Claims 18, 21-24, 26-28, 30-34, and 36-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beraud et al. WO 2004/108897 (effective filing date of June 2, 2003) and

Adessi et al., 2000, Solid Phase DNA Amplification: characterization of primer attachment and amplification mechanisms, Nucleic Acids Research, 28(20): e87, 8 pages.

For present claims 26-28 and 36-38, Beraud et al. teach methods comprising solid phase synthesis of DNA encoding siRNA, detaching the DNA from the solid phase, amplification via PCR, cloning into viral vectors, and packaging (please refer to the entire specification particularly paragraphs 5-10, 47-52, 57-58, 71-72, 78-79, 86-87, 92-95; Figures).

For present claim 18, Beraud et al. teach 10^6, 10^8, 10^9, or 2.7 x 10^{11} siRNA (please refer to the entire specification particularly paragraph 78 and 87).

For present claims 21-22, Beraud et al. teach retroviral and lentiviral expression vectors (please refer to the entire specification particularly paragraphs 71-72, 92-95).

For present claims 23-24, Beraud et al. teach siRNA (please refer to the entire specification particularly paragraphs 6).

For present claims 24, 30, 34, 36, and 37, Beraud et al. teach sense and antisense regions between 10-30, 15-25, 17-23, 19-21, or 19-23 nucleotides in length and single stranded portions of 1-5 nucleotides in length or loops of less than 10, 20, or 50 nucleotides in length (see paragraphs 61, 66 for example).

For present claims 31, 34, 36, and 37, Beraud et al. teach siRNA that target mammalian genes (see paragraph 64 for example).

For present claim 32, Beraud et al. teach MMTV, lentiviral vectors, adenoviral vectors, adeno-associated vectors, HIV vectors, MSCV vectors, MuLV vectors, etc. (see paragraphs 75, 92, 93, and 94 for example).

For present claims 33, Beraud et al. teach pol III and termination segments (see paragraphs 14-17, 42, and 48 for example).

However, while Bernaud et al. teach solid-phase synthesis on beads and oligonucleotides on microarrays, Bernard et al. does not specifically teach solid-phase synthesis on microarrays.

For present claims 26-27 and 36-37, Adessi et al. teach solid phase DNA amplification (i.e. combined synthesis and amplification steps; please refer to the entire reference particularly the abstract; Figures 1-2).

The claims would have been obvious because the substitution of one known element (i.e. bead based solid phase synthesis or bead as taught by Beraud et al.) for another (i.e. microarray based solid phase synthesis or glass slide as taught by Adessi et al.) would have yielded predictable results (i.e. solid-phase synthesis of oligonucleotides) to one of ordinary skill in the art at the time of the invention. See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

Arguments and Response

17. Applicants' arguments directed to the rejection under 35 USC 103 (a) as being unpatentable over Beraud et al. and Adessi et al. for claims 18, 21-24, 26-28, 30-34, and 36-38 were considered but are not persuasive for the following reasons.

Applicants contend that Adessi et al. alone does not teach a method for making a packaged viral vector effector library.

Applicants' arguments are not convincing since the teachings of Beraud et al. and Adessi et al. render the methods of the instant claims *prima facie* obvious.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Beraud et al. teach the limitations not taught by Adessi et al. (see rejection above).

Applicant's arguments fail to comply with 37 CFR 1.111(b) because they amount to a general allegation that the claims define a patentable invention without specifically pointing out how the language of the claims patentably distinguishes them from the references.

18. Claims 18, 21-24, 26-28, 30-34, and 36-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Caplan et al. US 2003/0149113 published August 7, 2003; Fosnaugh et al. U.S. 2003/0148507 published August 7, 2003; and Barone et al. U.S. Patent 7,026,114 (filing date of November 30, 1995 and effective filing date of September 13, 1995).

For present claims 26-28 and 36-38, Caplan et al. teach methods comprising solid phase synthesis of DNA encoding siRNA, cloning into viral vectors, and packaging (please refer to the entire specification particularly 23, 32, 47, 95-96, 179-186).

For present claims 21-22, Caplan et al. teach retroviral and lentiviral vectors (please refer to the entire specification particularly paragraphs 23, 184).

For present claims 23-24, Caplan et al. teach siRNA (please refer to the entire specification particularly paragraph 95).

For present claims 24, 30, 34, 36, and 37, Caplan et al. teach sense and antisense regions of about 17, about 18, about 19, about 21-23 nucleotides in length and loops 1-20, 4-10, or 6-8 nucleotides in length (see paragraphs 96, 179, 181 for example).

For present claims 31, 34, 36, and 37, Caplan et al. teach siRNA that target mammalian genes (see paragraphs 23, 96, 104 for example).

For present claim 32, Caplan et al. teach adenoviral vectors, adeno-associated vectors, etc. (see paragraph 184 for example).

For present claims 33, Caplan et al. teach pol III and stop codons (see paragraph 183 for example).

However, Caplan et al. does not teach a specific number of siRNA.

For present claims 18 and 26-27, Fosnaugh et al. teach an siRNA library comprising 4^{19} members, solid support synthesis of siRNA, cleaving of siRNA from the supports, and cloning into vectors incldiugn retroviral vectors (please refer to the entire specification particularly Figures 1 and 9; paragraphs 13-14, 25-26, 83, 91-94, 135-145, 153, 158-171).

However, while both Caplan et al. and Fosnaugh et al. teach solid-phase synthesis utilizing beads, while solid-phase synthesis utilizing a microarray is not taught.

For present claims 26-27, Barone et al. teach microarray based solid phase synthesis comprising synthesis of polymers including nucleic acids on supports including slides, cleavage of polymers form the support, and amplification via PCR (please refer to the entire specification particularly Figure 2; columns 2, 4, 10-11, 13, 20).

The claims would have been obvious because the substitution of one known element (i.e. bead based solid phase synthesis or bead as taught by Caplan et al. or Fosnaugh et al.; siRNA

population with an unknown size taught by Caplan et al.) for another (i.e. microarray based solid phase synthesis or glass slide as taught by Barone et al.; siRNA library of a specific size as taught by Fosnaugh et al.) would have yielded predictable results (i.e. solid-phase synthesis of oligonucleotides; potentially more diverse library; library of definitive size) to one of ordinary skill in the art at the time of the invention. See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

Arguments and Response

19. Applicants' arguments directed to the rejection under 35 USC 103 (a) as being unpatentable over Caplan et al., Fosnaugh et al., and Barone et al. for claims 18, 21-24, 26-28, 30-34, and 36-38 were considered but are not persuasive for the following reasons.

Applicants contend that the combination of Caplan et al., Fosnaugh et al., and Barone et al. do not teach the presently claimed methods.

Applicants' arguments are not convincing since the teachings of Caplan et al., Fosnaugh et al., and Barone et al. render the methods of the instant claims *prima facie* obvious. Please refer to the rejection above regarding the teachings of Caplan et al., Fosnaugh et al., and Barone et al.

Applicant's arguments fail to comply with 37 CFR 1.111(b) because they amount to a general allegation that the claims define a patentable invention without specifically pointing out how the language of the claims patentably distinguishes them from the references.

Conclusion

20. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Future Communications

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AMBER D. STEELE whose telephone number is (571)272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Amber D. Steele/
Primary Examiner, Art Unit 1639

September 15, 2009